

# Use of a Prostacyclin Analogue in Cholesterol Crystal Embolism

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The prognosis of cholesterol embolism is often poor, and no treatment is presently available. We report the use of a stable prostacyclin analogue in treating cholesterol embolism in a diabetic patient with arteriopathy. As a sole therapy, it improved cutaneous manifestations and pain, in parallel with an increased transcutaneous oxymetry. We think that prostacyclin analogues are novel candidates for the treatment of cholesterol embolism. © 1998 by John Wiley & Sons, Ltd.

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## Introduction

The ever-growing number of invasive vascular procedures and various anticoagulant treatments makes it necessary that the interest in cholesterol embolism, an underdiagnosed manifestation of atheromatous disease,<sup>1</sup> switches from the seasoned internist to all cardiovascular specialists and general physicians.<sup>2</sup> The arteriolar obstruction by cholesterol crystals dislodged from eroded plaques results in a broad spectrum of pictures, from cutaneous signs and muscular symptoms of the lower extremities to renal failure and life-threatening systemic manifestations. Most cases occur in patients with known vascular disease or prominent risk factors. However, precipitating factors are poorly understood, thus prevention is difficult, and there is, at present, no treatment of proven benefit.<sup>1–3</sup>

We report on the successful use of iloprost, a stable, potent prostacyclin analogue with vasodilator and antiaggregant properties,<sup>4</sup> in a patient with Type 2 diabetes mellitus with a clinical picture of acute cholesterol embolism.

## Case Report

A 72-year old man had had Type 2 diabetes mellitus for 25 years. He had documented peripheral arteriopathy and neuropathy. He was a non-smoker and had no history of hypertension, coronary insufficiency, cerebrovascular disease or nephropathy. He presented with dry gangrene of the great right toe, of 2 weeks' duration, and stable chronic ulceration of the great left toe, which had been present for 5 months. Doppler ultrasonography and transcutaneous oxymetry confirmed severe vascular insufficiency. Angiography (via the left femoral artery) showed

a significant stenosis of the right popliteal artery with no compensatory circulation, and a preocclusive left stenosis at the same level. Balloon angioplasty of the right popliteal artery was performed, and the necrotic right toe was resected three days later. The patient was put on complete bed rest and given intravenous antibiotic therapy, insulin infusion, buflomedil<sup>5</sup> and pentoxifylline. He did well initially, with improved circulation in the right limb as confirmed by sonography, but unchanged oximetry (Figure 1).

Two weeks after the vascular procedure, myalgia occurred suddenly in the right thigh and calf, associated with livedo reticularis on the plantar skin, painful petechiae, and severe cyanosis around the amputation area. Peripheral pulses and foot temperature remained unchanged. In the following hours to days, transient eosinophilia and elevated ESR were noted, serum complement levels remained within normal range, and no renal involvement or systemic manifestation were

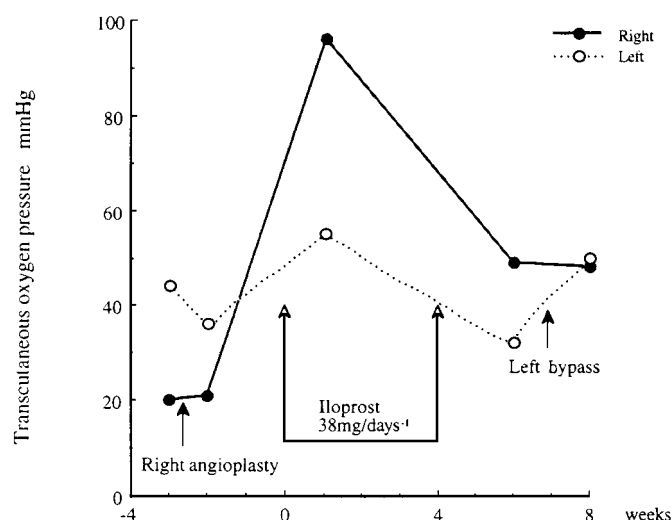


Figure 1. Effect of iloprost on transcutaneous oximetry

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observed. This constellation of signs and symptoms was strongly suggestive of cholesterol embolism.<sup>1</sup> Due to the severity of vascular disease, we refrained from biopsy in the right lower limb and attempted to treat by a prostacyclin analogue, while discontinuing previous antiaggregatory/vasodilator drugs. Iloprost (Schering, France) was administered intravenously at a dose of  $1.5 \text{ ng kg}^{-1} \text{ min}^{-1}$  for 6 h once a day for 4 weeks. The drug was well tolerated despite minor side-effects (headache, nausea). Both pain and cutaneous manifestations markedly improved after the first infusion of iloprost, in parallel with an increase in TCpO<sub>2</sub> (Figure 1), and the amputation area was almost healed on discharge. Three weeks later, a left popliteal artery bypass was successfully performed.

## Discussion

The clinical efficacy of prostacyclin or its stable analogues has been demonstrated in severe peripheral occlusive disease and Raynaud syndrome.<sup>4</sup> Preliminary information is available regarding the use of iloprost in myocardial ischaemia, cardiopulmonary bypass, and haemodialysis<sup>6</sup>. In addition, iloprost has been shown to improve the clinical status of diabetic patients with peripheral neuropathy.<sup>7</sup> The present observation suggests that it may also be effective in the treatment of cholesterol embolism. The mechanism of action of the drug remains to be investigated. Further studies are warranted to confirm

our finding and in order to know whether prostacyclin may improve the poor prognosis associated with repeated bouts of cholesterol embolism in non-diabetic as well as diabetic patients.

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